Citation:

Liou YA, King DJ, Zibrik D, Innis SM. Decreasing linoleic acid with constant alpha-linolenic acid in dietary fats increases (n-3) eicosapentaenoic acid in plasma phospholipids in healthy men. *J Nutr.* 2007 Apr;137(4):945-52.

PubMed ID: 17374659

Study Design:

Randomized Crossover Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

NEUTRAL: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare the effect of replacing vegetable oils high in linoleic acid with oils low in linoleic acid in foods, while maintaining constant alpha-linolenic acid, for 4 wk each, on plasma (n-3) fatty acids.

Inclusion Criteria:

- Non-vegetarian
- Nonsmoking men
- 20– 45 years of age
- BMI 18.5–29.9

Exclusion Criteria:

- Hypertension, hyperlipidemia, glucose intolerance, diabetes, or any other disease likely to affect lipid metabolism
- Consumption of any fatty acid, lipid or antioxidant supplements, or medications likely to interfere

Description of Study Protocol:

Recruitment

Recruitment methods not described.

Design: Randomized crossover trial

- Compare the effect of replacing vegetable oils high in LA with oils low in LA in foods, while maintaining constant ALA, for 4 wk each, on plasma (n-3) fatty acids.
- Nonvegetable sources of fat, except fish and seafoods, were unrestricted.
- Plasma phospholipid fatty acids at wk 0, 2, 4, 6, and 8, and triglycerides, cholesterol, serum CRP, and IL-6, and platelet aggregation were determined at wk 0, 4, and 8.

- LA and ALA intakes were 3.8 ± 0.12% and 1.0 ± 0.05%, and 10.5 ± 0.53% and 1.1 ± 0.06% energy with LA:ALA ratios of 4:0 and 10:1 during the low and high LA diets, respectively.

Blinding used (if applicable) Not reported

Intervention (if applicable)

- Low or high LA, with similar ALA such that 3 servings/d would result in a total dietary intake of ~1% of dietary energy as ALA.
- An oil blend containing 90 parts high oleic safflower oil or 90 parts high linoleic sunflower oil with 10 parts flax seed oil (Flax Canada 2015) was prepared and contained (g/100 g fatty acids) 13.7% LA and 6.5% ALA, or 56.5% LA and 6.9% ALA, with LA:ALA ratios of 2.1:1 and 8.2:1, respectively, for the high and low LA oil blends.
- Oleic acid was 69.5 and 24.2% fatty acids in the high and low LA blends, respectively.

Statistical Analysis

- Values are expressed as means ± SEM.
- The potential effects of the order in which the diets were consumed were tested before considering the effects of the high compared with low LA diet by ANOVA.
- Paired t tests were used to determine differences within the diet groups at the end of the two 4-wk diet periods.
- Tukey's test was used to determine differences due to time within a diet group, excluding the baseline (wk 0) value, which was not part of the controlled 8-wk diet period.
- Linear regression was used to assess the potential relation between the plasma phospholipid LA and EPA, the ARA:EPA ratio, and to assess the change in the plasma phospholipid DHA during the study.
- All statistical analyses were performed using SPSS software . Significance was determined at $P < 0.05$.

Data Collection Summary:

Timing of Measurements

- Plasma phospholipid fatty acids determined at wk 0, 2, 4, 6, and 8, and triglycerides, cholesterol, serum CRP, and IL-6, and platelet aggregation were determined at wk 0, 4, and 8.

Dependent Variables

-
  Plasma lipids, plasma phospholipids, inflammatory markers, and platelet aggregation

Independent Variables

- Compare the effect of replacing vegetable oils high in LA with oils low in LA in foods, while maintaining constant ALA, for 4 wk each, on plasma (n-3) fatty acids.
- Nonvegetable sources of fat, except fish and seafoods, were unrestricted.
  - LA and ALA intakes were 3.8 ± 0.12% and 1.0 ± 0.05%, and 10.5 ± 0.53% and 1.1 ± 0.06% energy with LA:ALA ratios of 4:0 and 10:1 during the low and high LA diets, respectively.

Control Variables

Description of Actual Data Sample:

Initial N: 24 men were enrolled

Attrition (final N): 22 men. 2 withdrew in the 1st 28 days of the study.

Age: 20-45 y of age, mean age 27.9 ± 1.1 years

Ethnicity: Not reported

Other relevant demographics:

Anthropometrics

Location: University of British Columbia, Canada

Summary of Results:

Key Findings

- The plasma phospholipid LA was higher and EPA was lower during the high than during the low LA diet period (P<0.001), but DHA declined over the 8-wk period (P < 0.001).
- The plasma phospholipid ARA:EPA ratios were (mean 6 SEM) 20.7 ± 1.52 and 12.9 ± 1.01 after 4 wk consuming the high or low LA diets, respectively (P <0.001).
- LA was inversely associated with EPA (P <0.001) but positively associated with ARA:EPA (P < 0.001).
- LA intake did not influence ALA, ARA, DPA, DHA or total, LDL or HDL cholesterol, CRP or IL-6, or platelet aggregation.

Other Findings

- The mean age, BMI, fasting plasma lipids, glucose or phospholipid fatty acids or triglycerides did not differ among the men randomized to 2 study groups.
- The mean fat intake from all sources was 32.5% total energy.
- The foods provided contributed ~55% of the total fat intake.
- Time effect results showed the levels of the major (n-6) and (n-3) fatty acids for the 2 groups of men (high LA–low LA and low LA–high LA), rather than the means for each of the high and low dietary LA periods.
- The plasma phospholipid total saturated fatty acids did not differ after 4 wk of consuming the high and low LA diets, but the total monounsaturated fatty acids, (n-3) fatty acids, and ARA:EPA ratio were higher, and the total (n-6) fatty acids was lower in the men after 4 wk of consuming the low LA compared with the high LA diet .
- The plasma phospholipid level of LA increased and EPA decreased during the 1st 2 wk of consuming the high LA diet, and LA decreased and EPA increased between 0 and 2 wk of consuming the low LA diet, with no further changes in these fatty acids with a continuation of the diet periods to wk 4.
- The men who consumed the low LA diet in the first 4 wk had a significant increase in their plasma phospholipid ALA level at wk 2, then a decrease in ALA at wk 4, whereas those men who consumed the low LA diet in the second 4 wk period had a higher plasma phospholipid ALA after 4 wk consuming the high LA diet.
- Plasma phospholipid DHA decreased (P <0.0001) at a rate of 0.104 g/(100 g plasma phospholipid fatty acids . wk).
- An association between the plasma phospholipid level of LA and the ARA:EPA ratio (P =0.0001, n =109). Plasma triacylglycerol fatty acids had higher LA and lower EPA after 4 wk of consuming the high compared with the low LA diet, with 17.4 ± 2.11 and 22.5 ± 2.08 g/100 g LA and 0.16 ± 0.02 and 0.13±0.02 g/100 EPA at wk 4 and 8, respectively, in the men randomized to the low LA–high

Author Conclusion:

In conclusion, high linoleic acid intakes decrease plasma phospholipid EPA and increase the ARA:EPA ratio, but do not favor higher ARA.

Reviewer Comments:

Relatively small sample size, only men studied. Diet periods only 4 weeks long.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions

1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions

1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes

1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	No
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A

4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	???
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	???
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes

7.5.	Was the measurement of effect at an appropriate level of precision?		Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?		???
7.7.	Were the measurements conducted consistently across groups?		Yes

8. Was the statistical analysis appropriate for the study design and type of outcome indicators? — Yes

8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	???
8.6.	Was clinical significance as well as statistical significance reported?	Yes
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A

9. Are conclusions supported by results with biases and limitations taken into consideration? — Yes

9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes

10. Is bias due to study's funding or sponsorship unlikely? — Yes

10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	???

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